3. Monazahian et al., *J. Med. Virol.*, (1999) 57(3): 223-229 (abstract enclosed); and
4. Agnello et al., *PNAS*, (1999) 96(22): 12766-12771 (entire article enclosed).

AMENDMENT

IN THE CLAIMS:

Please rewrite claim 7 in the following manner. The amendments to claim 7 are indicated in the attached Appendix.

7. (Thrice Amended) A method for inhibiting binding of the E2 protein of HCV to human cells comprising administering to a human infected with HCV an amount of a CD81 protein effective to bind HCV, wherein the CD81 protein comprises amino acids 113-201 of the human CD81 amino acid sequence depicted in SEQ ID NO: 21, to inhibit binding of HCV to human cells.

REMARKS

Introductory Comments

Claims 7, 29, 31, and 32 were examined in the Office Action under reply and rejected under 35 U.S.C. §112, first and second paragraphs. These rejections are believed to be overcome by the claim amendments and are otherwise traversed for reasons discussed below.

Overview of Claim Amendments

Claim 7 has been amended to claim the subject invention with greater particularity. Claim 7 now recites a method for administering CD81 to a "human infected with HCV." Also, amended claim 7 now recites administering CD81 "to inhibit binding of HCV to human cells."

Support for the foregoing amendments may be found throughout the specification and claims as filed, e.g., page 2, lines 27-29; page 8, lines 11-13; and Example 7, beginning at page 24.

The above amendments are made without intent to abandon any originally claimed subject matter, and without intent to acquiesce in any rejection of record.

Rejection Under 35 U.S.C. §112, Second Paragraph

The Examiner has asserted that "most recently amended" claim 7 is "indefinite because it is not clear how much, or if, the scope of the claim is intended to be altered." Office Action, page 2. Applicants disagree with the Examiner and assert that claim 7 is indeed definite.

35 U.S.C. §112, second paragraph mandates that the claims particularly point out and distinctly define the metes and bounds of the claimed subject matter, i.e., the claims must be definite. The standard to be used is "whether that scope of the claim is clear to a hypothetical person possessing the ordinary level of skill in the pertinent art." See MPEP §2171. Thus, the test is not as the Examiner describes it, i.e., "how much, or if, the scope of the claim is intended to be altered." Rather, the appropriate test is to evaluate whether the scope of amended claim 7 is clear to a hypothetical person possessing the ordinary level of skill in the pertinent art. Hence, Applicants respectfully request that the Examiner apply this test and identify any terms or portions of claim 7 that may be indefinite.

Further, case law and the MPEP allow Applicants to amend claims as necessary during prosecution. In particular, MPEP §2172, III, provides that the second paragraph of 35 U.S.C. §112 does not prohibit Applicants from changing what they regard as their invention during the pendency of the application. The Examiner contends that "it is not clear whether 'inhibiting binding' is intended to be any different from reducing infectivity and it is not clear whether 'an amount ... effective to bind HCV' is intended to be any different from a therapeutic amount." However, Applicants have the right to amend claims and need not explain the differences or similarities between terms used in original claims and the amended claims. Hence, Applicants respectfully request the withdrawal of this rejection.

The Examiner has rejected claim 7 as indefinite because "it lacks language that clearly correlates the outcome of the active step of the claim ... with the preamble ... ." In the interest of furthering prosecution, Applicants have amended claim 7 to recite "A method for inhibiting binding of HCV to human cells comprising administering to a human ... an amount of a CD81 protein ... to inhibit binding of HCV to human cells." The basis for this rejection is believed to be overcome and withdrawal thereof is respectfully requested.

Rejection Under 35 U.S.C. §112, First Paragraph

The Examiner has rejected claims 7, 29, 31, and 32 under 35 U.S.C. §112, first paragraph for lack of enablement. In particular, the Examiner states, "the specification does not teach that administration of a CD 81 protein that binds HCV in fact is of any therapeutic value or benefit to a human subject." Office Action, page 3. The Examiner cites the specification and several references and concludes that "one of skill in the art requires more than speculation and indeed requires factual evidence that a beneficial effect to a human patient is obtained by administration to a human of a CD81 protein." Office Action page 4.

Applicants respectfully submit that the present claims are indeed enabled. The Examiner appears to be asserting lack of enablement because the specification allegedly does not teach that administration of CD81 is beneficial to a human. However, the test for enablement is whether the experimentation needed to practice the invention is undue. See *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). It is not necessary to demonstrate that the invention is beneficial to a human to fulfill the enablement requirement. Hence, Applicants respectfully submit that the Examiner has presented a 35 U.S.C. §112, first paragraph rejection in error.

Moreover, the claims and written description comply with the utility requirements of 35 U.S.C. §101 and §112, first paragraph. For pharmacological or therapeutic inventions, the utility requirement is fulfilled if the invention provides any "immediate benefit to the public." See MPEP §2107.01. The MPEP further provides that "the mere identification of a pharmacological activity of a compound that is relevant to an asserted pharmacological use provides an immediate benefit to the public and satisfies the utility requirement." In the present application, the Applicants have cloned the DNA encoding an HCV receptor. The cloned DNA codes for a known cellular protein, CD81. Applicants have determined that CD81 binds the E2 portion of HCV. Applicants respectfully submit that identification of this binding activity satisfies the utility requirement.

Further, MPEP §2107.03 provides that "evidence of pharmacological or other biological activity of a compound will be relevant to an asserted therapeutic use if there is a reasonable correlation between the activity in question and the asserted utility." Applicants can provide arguments or reasoning to establish this reasonable correlation. The DNA cloned by the

inventors encodes a known human cellular protein CD81. CD81 acts as a receptor for HCV. One therapeutic mechanism of externally administered CD81 is to bind HCV, thereby decreasing the interaction of HCV with CD81 on human cells, thus preserving the usual function of CD81-positive human cells, as well as inhibiting viral infectivity. Therefore, there is a reasonable correlation between the activity, i.e., binding of CD81 to HCV, and the asserted utility, i.e., inhibiting binding of HCV to human cells (as CD81 is present on human cells).

The Examiner reasserts in this Office Action that there exists "no factual evidence of record that administering to a patient a CD81 protein that binds circulating HCV would eliminate or reduce the amount of available virus for interacting with any cell surface receptor." Office Action page 5. As mentioned above, it is not clear to Applicants why such evidence needs to be provided. Applicants believe that the claims are enabled and that the request for factual evidence by the Examiner is in error. Claim 7 recites a method for inhibiting binding of HCV to human cells. The inhibition of binding is achieved by administering CD81, the amount of CD81 administered being effective to inhibit binding of HCV to human cells. A person of skill in the art will have knowledge of the techniques necessary to administer CD81 to a human. The specification teaches techniques to quantify the binding of HCV to human cells and such techniques are also well known in the art. See Example 7 in Specification; Monazahian et al., *J. Med. Virol.*, (1999) 57(3): 223-229 (abstract enclosed); and Agnello et al., *PNAS*, (1999) 96(22): 12766-12771 (copy of entire article enclosed). Thus, a person of skill in the art is enabled to practice the invention, i.e., to administer CD81 to a human and quantify binding of HCV to human cells.

The Examiner states in conclusion: "Enablement for a method for using a protein as a pharmaceutical as claimed requires at least some factual basis for concluding that the *in vitro* results disclosed for CD81 protein can be extrapolated, with a reasonable expectation for success, to an *in vivo* benefit to a human patient." Office Action page 6. Case law and the MPEP do not require a factual basis for concluding that *in vitro* results can be extrapolated to an *in vivo* benefit. MPEP §2164.03 provides that results from an *in vitro* model in the specification constitute a working example if that example "correlates" with the claimed method. The specification includes a working example that demonstrates the binding of HCV to CD81. See Example 7 in the specification. As mentioned in the specification, the only animal model of HCV infection is a chimpanzee model and HCV does not readily propagate in tissue culture. As

testing the claimed method in the chimpanzee model would be expensive and time consuming, a person of skill in the art would accept that the *in vitro* data included in the specification could be used to predict a beneficial effect in a human. That is, a person of skill in the art would accept that the *in vitro* data is reasonably correlated to a beneficial effect in a human infected with HCV. Hence, Applicants believe that it is not necessary to provide a factual basis for correlating *in vitro* results with an *in vivo* benefit.

For the reasons presented above, Applicants believe that the pending claims are enabled. Hence, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §112, first paragraph.

CONCLUSION

Applicants respectfully submit that the claims are novel and nonobvious over the art and comply with the requirements of 35 U.S.C. §112. Accordingly, allowance is believed to be in order and an early notification to that effect would be appreciated.

Please direct all further communications in this application to:

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

Claim 7 has been amended as follows:

.7. (Thrice Amended) A method for inhibiting binding of the E2 protein of HCV to human cells comprising administering to a [patient] human infected with HCV an amount of a CD81 protein effective to bind HCV, wherein the CD81 protein comprises amino acids 113-201 of the human CD81 amino acid sequence depicted in SEQ ID NO: 21, to inhibit binding of HCV to human cells.